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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/488,728	01/20/00	TROUTT A	2623-B

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HM22/0731

EXAMINER
JIANG, D

ART UNIT	PAPER NUMBER
1646	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/488,728	Applicant(s) TROUTT, ANTHONY B	
	Examiner Dong Jiang	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicants' amendment filed on 5 July 2001 (paper No. 7) is acknowledged and entered. Following the amendment, the original claims 3-6 are canceled, and the new claims 13 and 14 are added. Currently claims 13 and 14 are pending and under consideration.

Formal Matters:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Double Patenting Rejections:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 13 and 14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5 and 7 of U.S. Patent No. 6,083,906. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. Claim 5 of the patent is directed to a method of treating osteoarthritis comprising administering an effective amount of soluble IL-17 receptor, and the limitations in the dependent claim 7 is directed to the extracellular domain of SEQ ID NO:2, or 4, and the variants and fragments thereof, which are identical to the limitations in claim 14 of the instant application. The method steps and the compositions used in the method of the patent are identical to those in claims 13 and 14 of the present invention, which are directed to a method of

treating or preventing ulcerative colitis, diabetes and Crohn's disease. The recited limitation in the preamble "a method of ... *preventing*" is noted. In searching the prior art, the results of record have not established that the claimed diseases can be predicted prior to the development of the disease. As so, the claim limitation reads on that any or all individuals can be prevented from the diseases, including those who have osteoarthritis as indicated in claim 5 of the U.S. patent. Therefore, the conflicting claims are not patentably distinct from each other.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is indefinite for reciting the limitation of "the GAP computer program" in part (c) of the claim. It is unclear what "the GAP computer program" is, which is used to determine the scope of the protein sequences in the claim. Therefore, metes and bounds of the claim cannot be unambiguously determined. It is suggested the recitation to be eliminated from the claim as such algorithm is no longer required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level

of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The specification discloses a method of treating osteoarthritis (OA) with a soluble IL-17 receptor (IL-17R), as the soluble IL-17R inhibits the production of nitric oxide (NO) by cartilage-associated cells from individuals afflicted with OA, and NO is known for its pathogenetic role in the disease (page 1, the last paragraph, and Example 2). As pointed out by the applicant, and used as the support for the present invention (see "Remarks" in the amendment in paper No. 7), that the prior art has shown that increased levels of nitric oxide (NO) occur in inflammatory diseases, i.e., arthritis, ulcerative colitis, diabetes, Crohn's disease, and inhibitors of NO synthetases (NOS) have been used in experimental models of inflammatory disease (page 2, lines 7-9). In conjunction with the fact that IL-17 stimulates production of nitric oxide (NO) by cartilage-associated cells in OA, the applicant, therefore, claims that IL-17R would be useful for treating diseases set forth above. However, the Examiner finds such deduction is not predictable because increased levels of NO is not IL-17-specific, and may be promoted by other factors, such as IL-1β, TNF-α, and LPS (page 2, lines 15-16), and IFN-γ is the most powerful inducer of NOS (Liew, CIBA Foundation Symposium, 1995, 195:234-44, the abstract). Therefore, the generalized idea of applying the soluble IL-17R to treat other diseases with elevated levels of NO, such as ulcerative colitis, diabetes, Crohn's disease, based upon the single example of OA is not convincing. The prior art reveals that IL-1β has a major role in inducing NO production and the pathogenesis of diabetes (Ankarcrona et al., Experimental cell research, 1994, 213: 172-177, the abstract and Figures 1 and 2). Neither the prior art nor the current disclosure has demonstrated an association of IL-17 to diseases listed in claim 13. In the absence of predictability of involvement of IL-17, it is unpredictable that the treatment of the diseases with soluble IL-17R would be beneficial. The specification provides neither clear direction or enough guidance, nor working example to teach how to use the method to treat any of the claimed diseases. Therefore, undue experimentation would be required when treating each of the diseases.

Given the reasons above, and the breadth of the claim in light of the nature of the invention which is a method of antagonizing IL-17, the state of the prior art of lack of support in IL-17 involvement in those diseases, the lack of predictability in the art, and the lack of direction or guidance and working examples for treating a disease listed in the claims with the soluble IL-17R, it would require undue experimentation for the skilled artisan to practice the invention as claimed.

Furthermore, even if the specification taught how to use the soluble IL-17R to treat the claimed diseases, enablement would not be commensurate in scope of "*preventing* an inflammatory diseases" as in claim 13, variants of the protein with at least about 70% identity and binding IL-17 as in part (c) of claim 14, and fragments of the protein as in part (d) of claim 14.

With respect to the claim limitation of *preventing* an inflammatory diseases, the prior art has not established that any of the diseases can be prevented as claimed. All that has been shown is that the diseases can be treated. To prevent the diseases, would necessarily mean that an individual would have to be first identified as at the risk before a disease develops, and then given the soluble IL-17R, and such administration would ensure that the individual did not develop the diseases. As neither the prior art nor the specification has established how to identify individuals who are "at risk for the disease", a method of preventing is void. Furthermore, the recitation in claim 13 that "administering an effective amount of *an interleukin-17 receptor*" reads on the full length molecule of IL-17R, and the specification does not teach how to use such a molecule, which is non-soluble, and not routinely purified, or used for therapeutic purposes, thus it is not predictable whether such non-soluble molecule would be applicable for the claimed method of use. Therefore, undue experimentation is required to determine such prior practicing the claimed invention.

With respect to parts (c) and (d) of claim 14, the specification discloses merely *two* amino acid sequences of IL-17R with particularity, murine IL-17R with SEQ ID NO:2, and human IL-17R with SEQ ID NO:4, and two specific fragments thereof. No other IL-17R variants or fragments meeting the limitations of the claim were ever identified. Part (c) of the claim is directed to a protein having 70% sequence identity to the extracellular domain of SEQ ID NO:2

or 4, and binding IL-17. The specification does not define structurally and functionally any variants of SEQ ID NO:2 or 4, or provide any specific guidance as to which regions of the proteins would be tolerant of variations and which would not regarding to retaining the functional activities of the polypeptides. In order to make a sequence variant, for instance, with the reasonable assurance that it would have the desirable property of the invention, such as binding IL-17, the artisan would need to know which regions of the disclosed molecule are responsible for the interaction underlying its biological function(s). The specification provides neither clear direction or enough guidance, nor working example to teach how to make a commensurate number of the claimed species. As so, it would require undue experimentation to practice the invention in a manner commensurate in scope with the claim.

Part (d) of claim 14 encompasses fragments of the protein in part (c). The specification provides no direction, guidance, or working example to teach how to make a commensurate number of the claimed species. It is in no way predictable that a randomly selected fragment of a protein having 70% sequence identity to the extracellular domain of SEQ ID NO:2 or 4, would afford a protein having activity comparable to the one disclosed (binding IL-17). Therefore, undue experimentation would be required of the skilled artisan to make the claimed invention in its full scope.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 13 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Yao et al, WO 96/29408.

Yao discloses a method for suppressing rejection of a grafted organ or tissue in a graft recipient using a soluble IL-17R having amino acid residues 1-322 of SEQ ID NO:2 or 1-320 of SEQ ID NO:10, which share the identical amino acid sequence with SEQ ID NO:2 or 4 of the present invention. The method steps and the compositions used in the method of the patent are

identical to those in claims 13 and 14 of the present invention. Although the method of the current invention is for treating and *preventing* ulcerative colitis, diabetes and Crohn's disease, the recited limitation of *preventing* would encompass any or all individuals, including those of graft recipients in Yao's invention, because the results of record from searching the prior art, have not established that the claimed diseases can be predicted prior to the development of the disease. As so, the claim limitation reads on that any or all individuals. Therefore, the reference anticipates the current claims.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

DJ
7/20/01